Best thing since sliced bread:
Using NHANES data to assess folic acid intake from supplements and food in the U.S. post-fortification

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Sources of folic acid

- **Enriched cereal-grain products (ECGP)**
  - Required fortification: 140 μg/100 g

- **Ready-to-eat (RTE) cereals**
  - Voluntary fortification up to 400 μg/serving

- **Dietary supplements (SUP)**
  - Up to 1,000 μg/dose
Recommended folic acid intake

- Daily maternal intake of 400 micrograms (µg) of folic acid prevents up to 70% of neural-tube defects.


- Women of childbearing potential are recommended to consume at least 400 µg of folic acid, the synthetic form of folate, daily from fortified foods, supplements, or both in addition to a diet high in folate rich foods

Tolerable Upper Intake Level (UL)

- Set for adults at 1,000 µg (1 mg) in 1998 by the Institute of Medicine
- No established direct toxic effects of folic acid in adults or children in any dosage
  - No dose-response
- UL established based on 5 mg dose and potential masking of symptoms of pernicious anemia among older adults
  - Divided by factor of 5 to ensure no one reaches 5 mg
- Recommendations for children derived from adult UL based solely on body weight

<table>
<thead>
<tr>
<th>Age</th>
<th>Tolerable upper intake level (usual intake; µg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–12 months</td>
<td>Not established</td>
</tr>
<tr>
<td>1–3 years</td>
<td>300 µg/day</td>
</tr>
<tr>
<td>4–8 years</td>
<td>400 µg/day</td>
</tr>
<tr>
<td>9–13 years</td>
<td>600 µg/day</td>
</tr>
<tr>
<td>14–18 years</td>
<td>800 µg/day</td>
</tr>
<tr>
<td>≥19 years</td>
<td>1,000 µg/day</td>
</tr>
</tbody>
</table>
METHODS
National Health and Nutrition Examination Survey (NHANES)

- Representative of U.S. civilian, non-institutionalized population
- Conducted in 2-year cycles
- Consists of interview and physical examination
- Nutrition data collected in 2 24-hour dietary recalls
  - 1st administered in person at the physical examination
  - 2nd administered 3–10 days later over the phone
- Supplement data collected as part of the interview
Total daily folic acid intake

- **Dietary folic acid (on each of 2 days):**
  - Twenty-four hour dietary recalls
  - Data on folic acid estimated from each food
  - Total dietary folic acid intake = Sum of folic acid consumed from each food during the previous 24 hours

- **Folic acid from supplements (over past 30 days):**
  - Detailed questionnaire and information from supplement bottles
  - Data on intake from each supplement estimated from:
    - Number of days supplement consumed
    - Amount consumed each day the supplement was consumed
    - Serving size
  - Average daily folic acid from supplements = Sum of folic acid consumed from each supplement over the past 30 days / 30

- **Total daily folic acid intake (on each of 2 days):**
  - Dietary folic acid (each day) + Average daily folic acid from supplements
### Categories of folic acid consumption

<table>
<thead>
<tr>
<th>Category</th>
<th>ECGP</th>
<th>RTE Cereal</th>
<th>Dietary Supplement</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECGP only</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>ECGP + RTE</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>ECGP + SUP</td>
<td>YES</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td>ECGP + RTE + SUP</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
</tbody>
</table>
Biomarkers of folate metabolism

- **Serum folate**
- **Red blood cell folate**
  - Indicator of long-term folate status
- **Serum vitamin B-12**
- **Plasma homocysteine**
  - Higher levels indicator not specific for either folate or vitamin B-12 deficiency
- **Methylmalonic acid**
  - Higher levels indicator specific for vitamin B-12 deficiency
Study populations

- **Women of childbearing age**
  - 15–44 years

- **Adults**
  - ≥19 years

- **Children**
  - 1–18 years

- **Exclusions**
  - Pregnant
  - Missing data
  - Poor dietary data quality
Analysis

- **Software for Intake Distribution Estimation (PC-SIDE)**
  - Allows estimation of *usual* intake accounting for variation in intake between people and variation in intake of individuals

- **SUDAAN / SPSS**
  - Takes into account complex sample survey design

- **Statistics estimated**
  - Population demographics
  - Median usual daily folic acid intake
  - Percentage meeting recommendations
  - Percentage in each intake category of folic acid consumption
  - Percentage with intake over the UL
  - Geometric mean biomarker levels
RESULTS

Women of childbearing age (15–44 years)
Women of childbearing age (15–44 years)
Usual total daily folic acid intake, N = 2,617

- **Median**
  - 245 µg (95% CI: 225, 265)

- **Percent achieving recommended daily intake (400 µg):**
  - 23.8% (95% CI: 20.3, 27.3)

- **Strongest association with achieving recommended folic acid intake:**
  - Taking a dietary supplement containing folic acid
    - 10.2 times more likely than non-users of supplements

NHANES 2003-2006
Women of childbearing age (15–44 years)
Use of dietary supplements containing folic acid
N = 2,617

- Percent taking dietary supplements containing folic acid
  - 31.7% (95% CI: 28.1, 35.4)

- Characteristics associated with supplement use
  - Age over 25 years
  - Higher education
  - Non-Hispanic white race/ethnicity
  - Note: Obesity and diabetes were NOT associated with supplement use, but are associated with increased risk for NTDs

NHANES 2003-2006
Women of childbearing age (15–44 years)  
Usual total daily total folic acid intake  
Stratified by supplement use, N = 2,617

- Users of dietary supplements containing folic acid
  - Median usual total daily intake: 502 µg (95% CI: 465, 539)
  - Percent achieving recommended intake: 72.0% (65.4, 78.5)

- Non-users of dietary supplements containing folic acid
  - Median usual total daily intake: 163 µg (150, 176)
  - Percent achieving recommended intake: 1.4% (0.5, 2.4)

NHANES 2003-2006
RESULTS

Adults aged ≥19 years
Folic acid intake in U.S. adults aged ≥19 years by race/ethnicity, age, and sex and folic acid consumption group, N = 8,258

**Race/ethnicity:**
- Mexican-American
- Non-Hispanic Black
- Non-Hispanic White

**Age, years:**
- 19-39
- 40-59
- ≥60

**Sex:**
- Female
- Male

NHANES 2003-2006
Percent of U.S. adults aged ≥ 19 years who consumed > UL of folic acid (FA) and the amount of folic acid from supplements, N = 8,258

<table>
<thead>
<tr>
<th>Source, average amount of folic acid from supplements</th>
<th>Folic acid-SUP µg/d</th>
<th>%</th>
<th>Median intake µg</th>
<th>Intake &gt;UL % ± SE</th>
<th>FA from supplements Mean ±SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECGP</td>
<td>0</td>
<td>42.5</td>
<td>138</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ECGP + RTE</td>
<td>0</td>
<td>18.2</td>
<td>274</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ECGP</td>
<td>&gt;0 – &lt;200</td>
<td>6.2</td>
<td>264</td>
<td>0</td>
<td>77.9 ± 5.2</td>
</tr>
<tr>
<td>ECGP + RTE</td>
<td>&gt;0 – &lt;200</td>
<td>3.8</td>
<td>439</td>
<td>0</td>
<td>91.0 ± 7.2</td>
</tr>
<tr>
<td>ECGP</td>
<td>201 – 400</td>
<td>14.9</td>
<td>496</td>
<td>0</td>
<td>371.1 ± 2.9</td>
</tr>
<tr>
<td>ECGP + RTE</td>
<td>201 – 400</td>
<td>8.6</td>
<td>665</td>
<td>0</td>
<td>376.3 ± 2.3</td>
</tr>
<tr>
<td>ECGP</td>
<td>&gt;400</td>
<td>3.9</td>
<td>931</td>
<td>39.4 ± 4.9</td>
<td>836.5 ± 35.2</td>
</tr>
<tr>
<td>ECGP + RTE</td>
<td>&gt;400</td>
<td>2.1</td>
<td>1119</td>
<td>67.6 ± 7.6</td>
<td>803.8 ± 33.8</td>
</tr>
</tbody>
</table>
Geometric mean* serum folate, red blood cell (RBC) folate, and homocysteine (HC), serum vitamin B-12, and methylmalonic acid (MMA) concentrations in U.S. adults aged ≥19 years by folic acid consumption group

<table>
<thead>
<tr>
<th>Category</th>
<th>N**</th>
<th>Serum folate [ng/mL] (95% CI)</th>
<th>RBC folate [ng/mL] (95% CI)</th>
<th>HC [μmol/L] (95% CI)</th>
<th>B-12 [pg/mL] (95% CI)</th>
<th>MMA [μmol/L] (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECGP only</td>
<td>3,337 (1,653)</td>
<td>9.4 (9.2, 9.6)</td>
<td>234 (230, 239)</td>
<td>8.8 (8.6, 8.9)</td>
<td>412 (401, 423)</td>
<td>0.143 (0.138, 0.149)</td>
</tr>
<tr>
<td>ECGP + RTE</td>
<td>1,385 (629)</td>
<td>12.1 (11.7, 12.5)</td>
<td>273 (266, 279)</td>
<td>8.3 (8.1, 8.4)</td>
<td>462 (449, 475)</td>
<td>0.146 (0.137, 0.156)</td>
</tr>
<tr>
<td>ECGP + SUP</td>
<td>1,754 (870)</td>
<td>14.6 (14.1, 15.2)</td>
<td>309 (303, 315)</td>
<td>7.9 (7.7, 8.1)</td>
<td>530 (514, 548)</td>
<td>0.131 (0.126, 0.135)</td>
</tr>
<tr>
<td>ECGP + RTE + SUP</td>
<td>1,004 (486)</td>
<td>16.9 (16.2, 17.6)</td>
<td>329 (321, 337)</td>
<td>7.7 (7.5, 7.8)</td>
<td>547 (525, 570)</td>
<td>0.129 (0.123, 0.136)</td>
</tr>
</tbody>
</table>

*Weighted and adjusted  
** Unweighted
RESULTS

Children aged 1–18 years
Percent of U.S. children aged 1–18 years who consumed different sources of folic acid by folic acid consumption group, N = 7,161

<table>
<thead>
<tr>
<th>Category</th>
<th>% who consumed folic acid (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECGP only</td>
<td>32.1 (29.9, 34.4)</td>
</tr>
<tr>
<td>ECGP + RTE</td>
<td>42.4 (39.9, 44.9)</td>
</tr>
<tr>
<td>ECGP + SUP</td>
<td>9.1 (7.7, 10.8)</td>
</tr>
<tr>
<td>ECGP + RTE + SUP</td>
<td>16.4 (14.3, 18.8)</td>
</tr>
</tbody>
</table>
### Median usual total daily folic acid intake in U.S. children by age and folic acid consumption group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>ECGP only</th>
<th>ECGP + RTE</th>
<th>ECGP + SUP</th>
<th>ECGP + RTE + SUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–3 years</td>
<td>n = 1,322</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4–8 years</td>
<td>n = 1,531</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9–13 years</td>
<td>n = 1,905</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14–18 years</td>
<td>n = 2,403</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NHANES 2003-2006**
Percent of U.S. children who consumed > recommended age-specific UL of folic acid by age
N = 7,161

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>UL (µg/day)</th>
<th>% total who consumed &gt;UL (SE)</th>
<th>% who consumed ECGP only &gt;UL (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–3</td>
<td>300</td>
<td>15.9 (1.9)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>4–8</td>
<td>400</td>
<td>27.0 (2.6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>9–13</td>
<td>600</td>
<td>3.6 (0.8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>14–18</td>
<td>800</td>
<td>0.9 (0.2)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>
Serum folate concentrations of U.S. children by age and folic acid consumption group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>ECGP only</th>
<th>ECGP + RTE</th>
<th>ECGP + SUP</th>
<th>ECGP + RTE + SUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–3 years</td>
<td>n = 830</td>
<td></td>
<td>n = 1,190</td>
<td>n = 1,690</td>
</tr>
<tr>
<td>4–8 years</td>
<td></td>
<td>n = 1,190</td>
<td></td>
<td>n = 1,690</td>
</tr>
<tr>
<td>9–13 years</td>
<td></td>
<td></td>
<td></td>
<td>n = 1,690</td>
</tr>
<tr>
<td>14–18 years</td>
<td></td>
<td></td>
<td></td>
<td>n = 1,690</td>
</tr>
</tbody>
</table>

NHANES 2003-2006
Median usual total daily folic acid intake per individual kilogram body weight of U.S. children by age

Median usual total daily folic acid intake by body weight, μg/kg/day

1–3 years, n = 916
4–8 years, n = 1,263
9–13 years, n = 1,751
14–18 years, n = 2,248

NHANES 2003-2006
Serum vitamin B-12 concentrations of U.S. children by age and folic acid consumption group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>ECGP only</th>
<th>ECGP + RTE</th>
<th>ECGP + SUP</th>
<th>ECGP + RTE + SUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–3 years</td>
<td>n = 830</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4–8 years</td>
<td>n = 1,190</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>9–13 years</td>
<td>n = 1,690</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14–18 years</td>
<td>n = 2,185</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adjusted geometric mean, pg/ml

NHANES 2003-2006
Conclusions
Women of childbearing age

- The majority of non-pregnant women of childbearing age consume less than the recommended level of folic acid (400 μg/day).

- Usual intake of the recommended level of folic acid is strongly associated with supplement use.
  - Prevalence of supplement use among this population varies by sociodemographic and other characteristics.

- Women with obesity or diabetes, two risk factors for neural tube defects, are NOT more likely to consume the recommended amount of folic acid.
Conclusions
Adults and children

- Supplements main contributor to higher folic acid intakes in U.S. adults
  - Adults who do not consume supplements are unlikely to exceed UL

- Only consumption of supplements at doses > 400 µg/day or consumption of multiple supplements is associated with intakes above the UL in U.S. adults

- Median usual total daily intake of folic acid increases in U.S. adults and children as the number of sources of folic acid increase

- At current fortification levels, U.S. children whose only consumption of folic acid is ECGP are unlikely to exceed their age-specific ULs
Conclusions
Adults and children

- Compared with consumption of ECGP only, consumption of RTE and supplements containing folic acid in U.S. adults is associated with:
  - Higher serum and RBC folate and vitamin B-12 concentrations
  - Lower homocysteine and MMA concentrations

- Compared with consumption of ECGP only, consumption of RTE and supplements containing folic acid in U.S. children is associated with:
  - Higher serum folate and vitamin B-12 concentration

- Sources of folic acid (e.g., ready-to-eat cereals or supplements) contain substantial amounts of vitamin B-12
**Strengths**

- Nationally representative
- Largest and longest-running national source of objectively measured health and nutrition data
- Oversample population subgroups
- Two 24-hour dietary recalls to estimate usual total folic acid intakes using established statistical method
Limitations

- Cross-sectional survey limits ability to examine associations between usual dietary intake and vitamin status
  - Dietary data collected at the time of the survey and 3–10 days after the survey may not reflect diet before the survey

- Average supplement intake may not reflect irregular patterns of intake

- Nutrient database may under- or overestimate actual folic acid intakes from fortified foods

- Sample size inadequate in some subgroups - unstable estimates
Acknowledgements

Helpful comments and suggestions from CDC, NCBDDD

• Joe Mulinare, Jorge Rosenthal, Cheryl Broussard, Yan Ping Qi, Jessica Marcinkevage

Co-Investigators:

• Lynn Bailey (University of Florida), Alicia Carriquiry (Iowa State University)
• CDC (RJ Berry, Mary Cogswell, Owen Devine, Heather Hamner, Christine Pfeiffer, Quanhe Yang)


Thank You

Questions?
# Usual total daily folic acid intake by category, U.S. adults aged ≥19 years, N = 8,258

<table>
<thead>
<tr>
<th>Category</th>
<th>Percent of study population</th>
<th>Usual total daily folic acid intake</th>
<th>Percent who consumed &gt;1000 µg/d (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Median, µg (25&lt;sup&gt;th&lt;/sup&gt; – 75&lt;sup&gt;th&lt;/sup&gt; percentile)</td>
<td></td>
</tr>
<tr>
<td>ECGP</td>
<td>42.2</td>
<td>138 (106 – 176)</td>
<td>0</td>
</tr>
<tr>
<td>ECGP+RTE</td>
<td>18.0</td>
<td>274 (230 – 324)</td>
<td>0</td>
</tr>
<tr>
<td>ECGP+SUP</td>
<td>25.2</td>
<td>479 (360 – 610)</td>
<td>5.5 (1.3)</td>
</tr>
<tr>
<td>ECGP+RTE+SUP</td>
<td>14.6</td>
<td>635 (512 – 797)</td>
<td>9.4 (2.0)</td>
</tr>
<tr>
<td>All Adults:</td>
<td>100.0</td>
<td>288 (160 – 462)</td>
<td>2.7 (0.4)</td>
</tr>
</tbody>
</table>

NHANES 2003-2006
Cumulative percent plots *usual* total daily folic acid intake, by source and supplement dose, U.S. adults ≥19 years.

Folic acid intake, micrograms

Folic acid from sup, μg: 0; >0 – 200; >200 – 400; >400

UL

median intake

NHANES 2003-2006
Additional outcomes – nutritional biochemistry

- **Folate status**
  - Serum folate concentrations
    - High >20 ng/ml
  - Red blood cell folate concentrations
  - Homocysteine concentration

- **Vitamin B-12 status**
  - Serum vitamin B-12 concentration
    - Low <300 pg/ml
  - Methylmalonic acid concentration
Additional statistical analyses – nutritional biochemistry

• Logarithmic transformations of serum vitamin concentrations: serum folate, RBC folate, homocysteine, vitamin B-12 and MMA

• Multiple linear regression models to estimate adjusted geometric means (least squares means) and 95% confidence intervals for serum vitamin concentrations

• Multiple logistic regression models to estimate adjusted prevalence (predictive margins) and 95% CI for high serum folate and low vitamin B12 concentrations

• All models adjusted for age, sex, race/ethnicity, smoking status, and body mass index. Models also stratified by age, sex, and race/ethnicity.

• SUDAAN statistical software used with examination center weights to account for the complex sampling design.
Percent of U.S. adults aged ≥19 years with high serum folate and low vitamin B-12 concentrations by category of folic acid consumption

<table>
<thead>
<tr>
<th>Category</th>
<th>Unweighted N</th>
<th>Serum folate &gt;20 ng/ml % (95% CI)</th>
<th>Vitamin B12 &lt;300 pg/ml % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECGP</td>
<td>3337</td>
<td>2.5 (1.7-3.4)</td>
<td>21.9 (19.1-24.7)</td>
</tr>
<tr>
<td>ECGP+RTE</td>
<td>1385</td>
<td>8.5 (6.5-10.6)</td>
<td>12.9 (10.6-15.1)</td>
</tr>
<tr>
<td>ECGP+SUP</td>
<td>1754</td>
<td>20.1 (17.1-23.1)</td>
<td>9.3 (7.2-11.4)</td>
</tr>
<tr>
<td>ECGP+RTE+SUP</td>
<td>1004</td>
<td>29.6 (25.4-33.7)</td>
<td>5.8 (3.7-7.9)</td>
</tr>
</tbody>
</table>

NHANES 2003-2006
Percent of U.S. children aged 1–18 y who reported consumption of different sources of folic acid, N = 7,161

- Folic Acid Enriched Cereal-Grain Products (ECGP) only: 32%
- Folic Acid Fortified “Ready-to-Eat” Breakfast Cereals (RTE): 59%
- Supplements containing Folic Acid (SUP): 26%
Percent of U.S. children who reported consumption of different sources of folic acid by age

ECGP only  | RTE  | Supplements

<table>
<thead>
<tr>
<th>1–3 years</th>
<th>4–8 years</th>
<th>9–13 years</th>
<th>14–18 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 1,322</td>
<td>N = 1,531</td>
<td>N = 1,905</td>
<td>N = 2,403</td>
</tr>
</tbody>
</table>

NHANES 2003-2006
Median usual total daily natural food folate intake in children by age and folic acid consumption group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>ECGP only</th>
<th>ECGP + RTE</th>
<th>ECGP + SUP</th>
<th>ECGP + RTE + SUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–3 years</td>
<td>132</td>
<td>145</td>
<td>155</td>
<td>165</td>
</tr>
<tr>
<td>4–8 years</td>
<td>1531</td>
<td>1648</td>
<td>1759</td>
<td>1867</td>
</tr>
<tr>
<td>9–13 years</td>
<td>1905</td>
<td>2012</td>
<td>2123</td>
<td>2230</td>
</tr>
<tr>
<td>14–18 years</td>
<td>2403</td>
<td>2515</td>
<td>2626</td>
<td>2731</td>
</tr>
</tbody>
</table>

n = number of participants

NHANES 2003–2006
## Usual total daily folic acid intake by source and age in US children aged 1-18 years

<table>
<thead>
<tr>
<th>Category</th>
<th>Usual total daily folic acid intake (Median, µg/day)</th>
<th>(25&lt;sup&gt;th&lt;/sup&gt; – 75&lt;sup&gt;th&lt;/sup&gt; percentile)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1–3 years, N=1,322</td>
<td>4–8 years, N=1,531</td>
</tr>
<tr>
<td><strong>ECGP</strong></td>
<td>81 (58 – 111)</td>
<td>132 (112 – 153)</td>
</tr>
<tr>
<td><strong>ECGP+RTE</strong></td>
<td>167 (142 – 197)</td>
<td>266 (226 – 316)</td>
</tr>
<tr>
<td><strong>ECGP+SUP</strong></td>
<td>271 (185 – 371)</td>
<td>342 (258 – 427)</td>
</tr>
<tr>
<td><strong>ECGP+RTE+SUP</strong></td>
<td>383 (310 – 461)</td>
<td>496 (390 – 634)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>176 (121 – 253)</td>
<td>292 (204 – 412)</td>
</tr>
</tbody>
</table>

NHANES 2003–2006
Percent of U.S. children with marginally low RBC folate or vitamin B-12 by folic acid consumption group

![Bar chart showing percent of U.S. children with marginally low RBC folate or vitamin B-12 by folic acid consumption group.](chart)

- **Source of Folic Acid**:
  - ECGP
  - ECGP+RTE
  - ECGP+SUP
  - ECGP+RTE+SUP

- **Parameters**:
  - Black bar: RBC folate <140 ng/ml
  - Red bar: Serum vitamin B12 <350 pg/ml

- **NHANES 2003-2006**

*Less than 0.2% met the definition of folate deficiency or low vitamin B-12 status*
Median usual total daily folic acid intake per individual kilogram body weight of U.S. children by age

- **1–3 years**: Median intake = 15 μg/kg/day (n = 916)
- **4–8 years**: Median intake = 14 μg/kg/day (n = 1,263)
- **9–13 years**: Median intake = 10 μg/kg/day (n = 1,751)
- **14–18 years**: Median intake = 6 μg/kg/day (n = 2,248)

**NHANES 2003-2006**
Public health implications  Children’s UL review

• No established direct toxic effects of folic acid in children in any dosage

• In 1998, IOM established the UL for adults

• IOM derived the children’s ULs based on body weight differences
Public health implications

- It is difficult for women of childbearing potential to achieve the recommended amount of folic acid without consuming a supplement; more effort is required to encourage all women, and in particular, women who are obese or have diabetes, to consume supplements with folic acid.

- Postfortification,
  - Consumption of enriched cereal-grain products alone or with RTE in U.S. adults is not associated with usual total daily folic acid intake > UL
  - Use of a daily supplement containing 400 µg or less in U.S. adults is not associated with intake > UL
  - Consumption of enriched cereal grain products alone in U.S. children is not associated with usual total daily folic acid intake > age-specific UL
Public health implications

- Since the ULs for children is not based on evidence of harm in children, it’s unclear what interpretations can be made when children exceed their age-specific UL.

- If fewer children consumed ready-to-eat cereals or supplements containing folic acid, or if supplements that are consumed by children contained less folic acid, the number of children with intakes that more than double their requirements might decrease.

- If there are concerns about higher intakes of folic acid in U.S. children, allowable levels of folic acid in ready-to-eat cereals and supplements may require further examination.